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The safety of radiofrequency ablation of the great saphenous vein in patients with previous venous thrombosis

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Background: **The safety of radiofrequency ablation (RFA) of the great saphenous vein (GSV) in patients with previous history of deep venous thrombosis (DVT) has not been determined.**

Methods: **From April 2003 to June 2006, 274 patients (68% women; mean age, 60 years ± 15 years) underwent 293 consecutive RFA procedures. In the first 15 months, the temperature probe was maintained at 85°C, with a pullback rate of 2 cm/min (85 limbs, 30%); we subsequently changed the protocol to 90°C and a pullback rate of 2 to 3 cm/min (205 limbs, 70%). We identified 29 patients (10%) with a history of DVT or duplex scan evidence of post-thrombotic venous disease; these were compared with the remaining 264 (90%). Postprocedural acute thrombotic (AT) events were analyzed. By the CEAP classification, 204 limbs (70%) were C_2 to C_4, and 89 (30%) were C_5 to C_6. Thirty-seven patients (13%) had a history of superficial thrombophlebitis (SVT). Proximal mean GSV diameter was 0.95 ± 0.29 cm (range, 0.4-2.3 cm). Concomitant procedures included avulsion phlebectomy in 88 limbs (30%) and perforator vein surgery in 4 (1%).**

Results: **AT events after RFA were detected in 38 limbs (13%), including thrombus protrusion into the sapheno-femoral junction (SFJ) in 24 (8%), common femoral vein in 7 (2.5%), and calf vein DVT in 7 (2.5%). Overall incidence of AT events in limbs with and without evidence of previous DVT was 7% (2 of 29) and 14% (36 of 264), respectively ($P = .36$). Variables significantly associated with AT events were previous SVT (10 of 37 [27%] vs 28 of 256 [11%], $P = .01$), a larger GSV diameter (mean 1.1 ± .39 vs 0.93 ± 0.27, $P < .01$), and first protocol (catheter temperature of 85°C with a slower pullback rate in 18 of 88 [20%] vs 20 of 205 [9.7%], $P = .02$). Concomitant venous operations were associated with an increase in AT events (23% vs 9%; $P < .002$). By multivariate analysis, larger proximal GSV diameter and previous SVT remained independently statistically significant ($P = .049$ and $P = .0135$, respectively). All AT patients were successfully treated with standard anticoagulation. No pulmonary emboli occurred.**

Conclusion: **RFA of the GSV in patients with previous venous thromboembolic events is safe and should be offered as an alternative to surgical procedures. These data demonstrate that AT events increase when larger-diameter GSVs are treated. (J Vasc Surg 2009;49:1248-55.)**

Great saphenous vein (GSV) reflux is important in the development of signs and symptoms of chronic venous insufficiency.[1] Radiofrequency ablation (RFA) of the GSV was introduced as a minimally invasive alternative to stripping, with the aim of interrupting venous flow through the incompetent GSV. This technique is relatively simple to perform and is associated with high patient satisfaction and an earlier return to work compared with traditional stripping.[2]

Although the main mechanism of action of RFA is vein spasm and collagen shrinkage by delivery of thermal energy, thrombus formation within the GSV has been described.[3] Deep venous thrombosis (DVT) after RFA of the GSV has been reported with a variable incidence of 0% to 16%.[2-7] Many authors consider a history of venous thromboembolic events is a risk factor for development of DVT after endovenous GSV ablation because this group of patients is generally excluded from studies.[2,8-10] The aim of this study was to evaluate the safety of RFA of the GSV in patients with previous venous thrombotic events.

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METHODS

Patients. During the 38 months from April 2003 to June 2006, we performed 293 consecutive RFA procedures on the GSV in 274 patients who were available for 1 week of follow-up. The Institutional Review Board approved the retrospective chart review of patients who underwent GSV ablation. During the same time period, we also performed 62 GSV stripping procedures for the treatment of symptomatic GSV reflux. Criteria for performing stripping vs RFA included known allergic reactions to local anesthetics, presence of a pacemaker or a defibrillator, inability to cannulate the GSV due to excessive tortuosity or a postphlebitic vein, early recanalization after RFA, and the patient's preference.

All limbs were classified according to the CEAP[11] classification: 204 limbs (70%) were C_2 to C_4 and 89 (30%) were C_5 to C_6 (healed or active venous ulcers). Indication for treatment of GSV reflux was any clinical stage of symptomatic venous insufficiency that did not improve after a trial of compressive therapy. Patients with a well-known history of lower extremity venous thromboembolic events

included those who (1) had been treated at our institution for DVT, with medical records available to document the event, (2) by history had a DVT that was treated by standard anticoagulation, or a DVT/pulmonary embolism (PE), or a DVT necessitating an inferior vena cava (IVC) filter, or (3) had a history of venous clot and duplex evidence of post-thrombotic changes in the examined deep veins.

Demographics, procedural data, and duplex scan findings were retrospectively collected and analyzed.

Duplex study. Preoperative and postoperative duplex scans were performed in our accredited noninvasive laboratory by registered vascular technologists using high-resolution color duplex scanners (HDI 5000 with Sono-CT option, Philips, Bothell, Wash). Veins were examined in the transverse and longitudinal views. All examinations were recorded on videotape and interpreted by an attending vascular surgeon. Interrogation of the superficial and deep venous systems included the GSV, small saphenous vein (SSV), common femoral vein (CFV), femoral vein, popliteal vein, and calf veins.

Venous segments were considered incompetent if reversed flow lasted >0.5 seconds in the standing position after manual compression and release. Standardized criteria for the diagnosis of acute DVT included diminished or absent color Doppler signals with respiration or augmentation maneuvers, echogenic signals within the vein lumen either partially or completely occluding the vessel, inability to compress the vein by pressure on the transducer, and dilated veins where thrombus was suspected.[12]

Once a DVT diagnosis was made, all vein segments involved were recorded. Post-thrombotic changes in examined veins were identified as obstructed or narrowed veins with thickened wall and reduced compressibility, intraluminal webs, hyperechoic material, multiple channels, and partly destroyed, thickened valves, as well as increased venous collaterals.[13,14] Perforator incompetence was not routinely investigated.

Technique. RFA of the GSV was performed according to the guidelines recommended by the manufacturer (VNUS Medical Technologies Inc, San Jose, Calif). The procedures were performed by three different vascular surgeons in collaboration with a physician/senior RVT (N. M.) according to a standardized protocol. The GSV was punctured under ultrasound guidance about the knee level, and an introducer sheath was advanced over a J wire; the RFA catheter was then positioned in the GSV, 1 cm distal to the superficial epigastric vein.

Tumescent anesthesia (400 mL of normal saline mixed with a 40 mL solution of 1% lidocaine, with 1:100,000 epinephrine and 5 mL of 7.5% sodium bicarbonate solution) was infiltrated around the target vein to obtain vein wall apposition and to reduce heat dissipation to the perivenous tissues. A continuous drip of heparinized solution (5000 U of heparin in 500 mL of normal saline) was infused through the tip of the RFA catheter at a rate of approximately 1 drop/s.

During the first 12 months of the study period, these procedures were performed in the hospital under general or spinal anesthesia. Combined procedures included stab-avulsion phlebectomies in 126 limbs (43%) and concomitant perforator interruption in four patients (1%) with long-standing nonhealing leg ulcers and perforators/GSV reflux deemed fit for surgery.

In the last 16 months (167 limbs, 57%), the RFA was changed to an outpatient, office-based procedure and was performed without concomitant procedures and under local and tumescent anesthesia only, without additional sedation. The temperature probe was maintained at 85°C with a pullback rate of 2 cm/min in the first 15 months of the study period (85 limbs, 30%). We subsequently switched to a temperature of 90°C with a pullback rate of 2 to 3 cm/min (205 limbs, 70%). A 6F catheter was used in 195 limbs and an 8F in 35 (data available on 231 limbs).

At the end of the procedure, all treated veins were imaged to confirm complete GSV closure and rule out extension of thrombus into the CFV. An ACE compressive bandage (BD, Franklin, NJ) was then applied from toes to groin to be maintained for the next 48 hours. Patients were encouraged to walk as soon as possible, with no significant limitations, and discharged home the same day.

We did not administer perioperative DVT prophylaxis drugs. If patients were already receiving an anticoagulant regimen, this was held for 5 days preoperatively and resumed after the procedure. This was done to decrease the risk that hematomas would develop after possible inadvertent vein perforations and at the catheter access site or at the sites of tumescent anesthesia infiltration. Laboratory evaluation of thrombophilia in patients with previous DVT was not routine.

Follow-up. Postoperative duplex scanning and clinical evaluation was routinely obtained at a mean of 5.8 ± 1.8 days in all except eight patients, who were excluded from the study. Patients were asked to return at 1 to 2 months and 6 months, but compliance was limited by the characteristics of this particular patient population (age, comorbidities, social-cultural background). Therefore, further follow-up ≤1 year after the procedure was possible in 190 limbs (65%) at a mean of 53.5 ± 66 days (median, 22 days).

Our follow-up protocol included duplex evaluation of all superficial and deep vein segments of both lower extremities, including the tibial, peroneal, and calf muscle veins. Obliterated GSVs appeared as noncompressible veins with thickened wall and absence of venous flow, sometimes filled with thrombus up to the sapheno-femoral junction (SFJ). The study end point of acute thrombotic (AT) events was defined as presence of DVT in any lower extremity segment or a tail of thrombus extending proximally from the GSV anywhere into the SFJ.

Management of AT events. In our early experience, all patients with AT events received standard anticoagulation therapy by unfractionated intravenous heparin or enoxaparin, followed by warfarin at standard doses. Treatment was continued until resolution of thrombus in case of SFJ thrombi; all other patients with DVT were treated with

standard anticoagulation of 3 to 6 months. At the beginning of this series, patients who exhibited thrombus abutting into the SFJ or CFV that appeared to be free floating were managed by placement of an IVC filter. As we noticed that all proximal thrombi after RFA resolved ≤2 weeks of anticoagulation, we arbitrarily changed our management policy and reserved caval filtration to patients who exhibited thrombus persistence for >1 week or progression.[4]

Statistical analysis. Data were collected retrospectively and entered into an electronic database. Patients with a well-known history of lower extremity venous thromboembolic events, or duplex scan evidence of it, were compared with the rest of the series. Comparisons between two groups of data were performed with the two-tailed Fisher exact test or χ^2 test for categoric variables, as appropriate. The Wilcoxon rank test was used for continuous variables. A value of $P < .05$ was considered statistically significant.

RESULTS

Bilateral procedures were done in 19 of 274 patients at different time intervals, comprising 152 left limbs (52%) and 141 right (48%). There were 185 women (68%) and 89 men (32%), with a mean age of 60 ± 15 years. All limbs had documented GSV reflux. Deep venous reflux was observed in 200 of 272 limbs (73%) available for examination and was localized in the CFV in 112 (41%), the femoral vein in 37 (14%), and the popliteal vein in 161 (59%).

Evidence of a previous DVT was found in 29 of 293 limbs (10%), comprising ipsilateral in 22, contralateral in six, and bilateral in one. Superficial thrombophlebitis (SVT) had occurred in 37 (13%) and was ipsilateral in 34, contralateral in two and bilateral in one.

The proximal GSV mean diameter was 0.95 ± 0.29 cm (range, 0.4-2.3 cm), and the mid-GSV mean diameter was 0.86 ± 0.99 cm (range 0.2-2.03 cm). Veins treated with the 6F catheter had proximal and mid-GSV mean diameters of 0.97 ± 0.02 cm and 0.87 ± 0.07 cm, respectively; veins treated with the 8F catheter had a proximal and mid-GSV mean diameters of 0.92 ± 0.05 cm and 0.9 ± 0.18 cm, respectively ($P = .32$ and $P = .88$, respectively).

Concomitant venous procedures were performed in 90 patients and included avulsion phlebectomy alone in 86 limbs (29), perforator vein surgery alone in 2 (0.7%) and both, phlebectomy and perforator surgery, in 2 (0.7%); these included three subfascial endoscopic perforator vein procedures and one open perforator interruption.

Age, gender, clinical presentation, presence of preoperative deep vein reflux, catheter size, and temperature were not significantly different between limbs with previous DVT and the rest of the limbs (Table I). However, limbs with previous DVT had also a higher incidence of previous SVT (10 of 37 [27%] vs 19 of 256 [7%], $P = .001$) and a smaller GSV diameter (0.84 ± 0.06 vs 0.96 ± 0.02, $P = .04$). Concomitant venous procedures were performed more often in patients without previous DVT (87 of 264 [33%] vs 3 of 29 [10%], $P = .01$).

The overall incidence of AT after RFA was 13% (38 of 293 limbs) and included thrombus protrusion into the SFJ in 24 (8%), CFV thrombus in seven (2.5%), and calf muscle veins thrombus in seven (2.5%). On univariate analysis a number of factors reached statistical significance (Table II). AT events occurred in 7% (2 of 29) of patients with previous DVT and in 14% (36 of 264) without previous DVT ($P = .36$). These AT events were not identified on the intraoperative completion duplex, but all were found on duplex follow-up. No clinically evident PE or other significant postoperative complication occurred in this series. More advanced clinical stages (combined classes 5 and 6 of CEAP) was not a predictive factor for development of AT events (15 of 38 [39%] vs 74 of 255 [29%], $P = .19$).

Concomitant venous operations were associated with a significant increase in AT events (20 of 90 [22%] vs 18 of 203 [9%]; $P < .01$); more so after avulsion phlebectomies ($P < .001$). Concurrent stab avulsion of varicosities did not influence anatomic location of AT events ($P = .84$). AT events did not develop in the three patients with previous DVT who underwent concomitant procedures.

Other variables significantly associated with AT events were previous SVT (10/37 [27%] vs. 28/256 [11%], $P = .01$), a larger GSV diameter (mean 1.1 ± 0.39 vs 0.93 ± 0.27, $P < .01$), catheter temperature of 85°C, and slower pullback rate of the first treatment protocol compared with the second treatment protocol (18/88 [20%] vs 20/205 [9.7%], $P = .02$). Catheter size (6F vs 8F) did not affect the rate of AT events (15% vs 12%, $P = .79$).

On multivariate analysis, only two variables—larger proximal GSV diameter and previous SVT—remained independently statistically significant ($P = .049$ and $P = .0135$, respectively).

AT events were treated with standard anticoagulation. Eight patients (21%) received an IVC filter, five were permanent, and three were temporary; of which two were removed at 17 and 22 days, respectively.

Of the 38 patients with duplex evidence of AT events, 36 (95%) were compliant with follow-up and underwent at least one further duplex scan after the initial diagnosis. Complete resolution of thrombus was demonstrated in 30 of 36 cases (83%) at a mean of 15.5 ± 18.2 days (range, 2-60 days), and partial resolution was evident in two (6%) at 5 and 13 days, respectively. In the remaining three patients, thrombus appearance (2 in the calf muscle veins and 1 in the CFV) did not improve within the first 2 months after diagnosis; pain and edema developed in two during follow-up, suggestive for post-thrombotic syndrome. Thrombus resolved in the eight patients who had received an IVC filter; in this group, the mean interval between detection of AT events and resolution of thrombus was 14 ± 7.5 days.

DISCUSSION

The operative treatment of symptomatic saphenous vein insufficiency has evolved from surgical elimination of the source of reflux—GSV stripping—to less invasive endovenous therapies—RFA and endovenous laser ablation (EVLA)—where the vein is left in place but excluded from the venous circulation. The main advantages of these endovenous techniques compared with stripping are reduced

Table I. Comparison of demographic and clinical data of 293 limbs (274 patients) with (n = 29) and without (n = 264) previous deep venous thrombosis undergoing great saphenous vein radiofrequency ablation

Variable	*No.*	*Previous DVT*	*No previous DVT*	P[a]
Total limbs, No. (%)	293	29 (10)	264 (90)	
Age, mean ± SD, y		63 ± 2.6	59.8 ± 0.9	.25
Sex, No. (%)				
Females[b]	198	19 (65)	179 (68)	.83
Males	95	10 (35)	85 (32)	
CEAP clinical presentation, No. (%)				
C_2-C_4	204	17 (58)	187 (71)	.2
C_5-C_6	89	12 (42)	77 (29)	
Previous SVT, No. (%)				
No	256	19 (65)	237 (90)	.001
Yes	37	10 (35)	27 (10)	
Prox GSV diameter, mean ± SD cm[c]		0.84 ± 0.25	0.96 ± 0.29	.04
Deep reflux, No. (%)[d]				
No	72	6 (21)	66 (27)	.65
Yes	200	22 (79)	178 (73)	
CFV	112	10 (35)	102 (38)	.69
FV	37	4 (14)	33 (13)	.9
PV	161	18 (62)	143 (54)	.69
Concomitant procedures, No. (%)				
No	203	26 (90)	177 (67)	.01
Yes	90	3 (10)	87 (33)	
Perforator interruption	4	1 (3)	3 (1)	.34
Phlebectomies	88	2 (7)	86 (33)	<.001
Catheter size, No. (%)[e]				
6F	195	16 (80)	179 (85)	.51
8F	35	4 (20)	31 (15)	
Catheter temp/pullback, No. (%)[f]				.3
85°C at 2 cm/min	88	6 (21)	82 (31)	
90°C at 2-3 cm/min	205	23 (79)	182 (69)	

CFV, Common femoral vein; *DVT,* deep venous thrombosis; *FV,* femoral vein; *GSV*, great saphenous vein; *PV,* popliteal vein; *SVT,* superficial vein thrombosis.
[a]Values of $P < .05$ are statistically significant.
[b]For statistical purposes, limbs were calculated as patients.
[c]Range was 0.4 to 2.3 cm for both groups.
[d]A total of 272 limbs were available for examination of the deep vein system.
[e]Data were available for 230 limbs.
[f]85°C was used during the first treatment protocol (first 15 months of the study); 90°C was used during the second treatment protocol.

postoperative pain, improved quality of life, and earlier return to work.[2] At our institution, patients can chose between RFA and stripping. No prospective studies have compared RFA with EVLA, but retrospective studies[5,15] show similar efficacy and safety profile. It should be noted, however, that the advantages of endovenous procedures over stripping have been limited to short-term results, not long-term recurrence or future complications.

The prevalence of DVT after saphenous RFA is believed to be 0.2% to 1%.[2,3,7] Some reports,[4-6] including one by our group,[4] have described a significantly higher risk of AT events of 8% to 16%. As expected, these reports have been the subject of significant controversy.[16-18]

This is a retrospective, observational study that includes our experience with GSV RFA during a 3-year period (2003-2006). Our technique of performing RFA carefully followed the recommendations of the manufacturer and was observed by company representatives after publication of our initial data. No significant flaws were observed, and no improvements in techniques were deemed necessary.

Our incidence of AT events has decreased significantly over the years and with a change in protocol, thus indicating that this adverse occurrence might have been partly linked to the learning curve. The rate of AT events was significantly higher in the first treatment protocol (85°C and slower pullback rate) compared with the second protocol (90°C and faster pullback rate). It is also possible that lower temperatures result in incomplete vein damage and thrombus formation, whereas higher temperatures may result in improved denaturation of the vein wall and endothelial injury with ablation of the vein by shrinkage rather than thrombus formation. In some other cases, close proximity of the RFA catheter to the SFJ could have been responsible for these thrombotic events.

Higher incidence of DVT in this series may also be due to older age compared with patients in other reports, as previously reported,[4,5] and to the larger diameter of treated GSVs. However, because we were unable to demonstrate a statistically significant association between older age and AT events, we do not believe there is currently enough evidence to just exclude these patients from a treatment they may significantly benefit from. Rather, these patients should be encouraged to ambulate immediately after the procedure, given ade-

Table II. Univariate analysis of risk factors for development of acute thrombotic events after great saphenous vein radiofrequency ablation in 293 limbs

Variable	*Total No.*	*AT events*	*No AT events*	P[a]
Limbs, No. (%)	293	38 (13)	255 (87)	
Age, mean ± SD, y		57.4 ± 2.5	60.6 ± 1	.19
Sex, No. (%)				
Females[b]	198	29 (76)	169 (66)	.27
Males	95	9 (24)	86 (34)	
CEAP presentation, No. (%)				
C_2-C_4	204	23 (61)	181 (71)	.19
C_5-C_6	89	15 (39)	74 (29)	
Prox GSV diameter, mean ± SD, cm[c]		1.1 ± 0.39	0.93 ± 0.27	<.01
Previous SVT, No. (%)				
No	256	28 (74)	228 (89)	.01
Yes	37	10 (26)	27 (11)	
Previous DVT, No. (%)				
No	264	36 (95)	228 (89)	.36
Yes	29	2 (5)	27 (11)	
Deep reflux, No. (%)[d]				
No	72	4 (36)	68 (33)	.06
Yes	200	28 (74)	172 (67)	
CFV	112	15 (39)	97 (38)	.57
FV	37	6 (16)	31 (12)	.4
PV	161	22 (58)	139 (55)	.26
Concomitant procedures, No. (%)				
No	203	18 (47)	185 (73)	<.01
Yes	90	20 (53)	70 (27)	
Perforator interruption	4	2 (5)	2 (1)	.08
Phlebectomies	88	20 (53)	68 (27)	<.001
Catheter size, No. (%)[e]				
6F	195	29 (88)	166 (84)	.8
8F	35	4 (12)	31 (16)	
Mean catheter temp/pullback, No. (%)[f]				.02
85°C at 2 cm/min	88	18 (47)	70 (27)	
90°C at 2-3 cm/min	205	20 (53)	185 (73)	

AT, Acute thrombotic; *CFV,* common femoral vein; *DVT,* deep venous thrombosis; *FV,* femoral vein; *GSV,* great saphenous vein; *PV,* popliteal vein; *SVT,* superficial vein thrombosis.

[a]Values of $P < .05$ are significant.

[b]For statistical purposes, limbs were calculated as patients.

[c]Range was 0.4 to 2.3 cm for both groups.

[d]272 limbs were available for examination of the deep vein system.

[e]Data were available for 230 limbs.

[f]85°C was used during the first treatment protocol (first 15 months of the study); 90°C was used for the second treatment protocol.

quate pain control, and monitored at closer time intervals.

We did not exclude large veins from RFA treatment. The proximal GSV mean diameter was 0.95 ± 0.29 cm (range, 0.4-2.3 cm) and mid-GSV mean diameter was 0.86 ± 0.99 cm (range, 0.2-2.03). Although several studies[2,19] on RFA initially excluded patients with a GSV diameter >1.2 cm, other authors did not consider large vein diameter an exclusion criteria for study enrollment and successfully treated them.[9,10,20] Exclusion for saphenous vein diameters >1.2 was initially established as a conservative measure but was later discontinued after reports of routinely successful treatment. Detailed results of RFA for large veins have been reported by Merchant et al[21,22] on a 5-year, multicenter study: of 39 veins with a diameter >1.2 cm (range, 1.2-2.4 cm), occlusion rates were 97% at 1 week and 93% at 6 months.

The increased rate of thrombus in the proximal GSV extending into the SFJ or CFV in cases of GSVs with large proximal diameters might have been the result of inadequate delivery of tumescent anesthesia and insufficient compression of the GSV at the SFJ. Incomplete wall apposition may lead to excessive heating of blood and thrombotic occlusion of the vein rather than collagen shrinkage. Furthermore, inadequate heating of the vein wall due to larger endothelial surfaces to be treated may increase collagen exposure from underneath a denuded endothelium and promote thrombus formation. To effectively occlude a large-diameter vein, we now pay particular attention at injecting additional tumescent infiltration in the perivenous tissues until we obtain a "dry" vein.

Although extension of thrombus from the GSV into the SFJ and formal DVTs both have been reported, few authors actually described in detail their postoperative duplex scan protocol. We grouped all AT events because we believed that they all could potentially be the source of PE and should be treated accordingly. In their early experience with endovenous ablation techniques, some authors have

used suction thrombectomy of floating thrombus in the CFV to avert long-term anticoagulation,[23] whereas others, like our group, used IVC filtration.[6] It is possible that the natural history of an untreated SFJ thrombus is rapid fibrinolysis and thrombus resolution, or subclinical PE; unfortunately, there are no prospective studies to support this hypothesis.

A case of PE that was associated with a SFJ thrombus extension and was not a true DVT has been reported.[24] On the other hand, in light of increased experience with the procedure and given the small number of clinically significant PE events reported in the literature, aggressive use of systemic anticoagulation or IVC filtration is likely not necessary in most patients. As others have suggested,[25] we have more recently tended to treat SFJ thrombus extension with antiplatelet therapy rather than anticoagulation until resolution. In the other patients, any further proximal extension of a DVT documented by repeat duplex ultrasound study is a significant risk factor for PE[12] and should be treated with standard anticoagulation.

If we were only to report on CFV DVTs, our incidence of this complication would have been 2%, slightly higher than otherwise previously reported.[8,22,26] Some may argue that what we considered as a worrisome proximal extension of GSV thrombus into the SFJ is an otherwise normal postoperative finding and not to be treated or mentioned. Duplex ultrasound imaging is certainly considered a reliable, reproducible, and validated tool for diagnosing venous system abnormalities; but it is important to point out how these endovenous techniques are relatively new techniques. Therefore, duplex findings after these procedures still need to be classified and correlated with clinical outcomes.

Furthermore, occurrence of PE after RFA without a detectable source of embolus at postoperative duplex scans has been reported.[27,28] We do not think that enough data are available to absolutely exclude proximal extension of GSV thrombus as a potential source of PE. Risk of PE after endovenous GSV ablation is extremely low, but is not exactly nil; several reports have described this serious complication.[22,24,26-30] Some patients have died: at least four deaths after endovenous GSV ablation procedures are posted on the Manufacturer & User Facility Device Experience (MAUDE) database maintained by the United States Food and Drug Administration.[28] It is unclear from the descriptions of some studies whether extensions of thrombus from the SFJ or true DVTs caused the PE.

The mechanism of proximal thrombus extension after RFA is unclear. Thermal or mechanical endothelial damage caused by the catheter itself might lead to thrombus formation at the SFJ in the postoperative period. Earlier reports[31] described prophylactic ligation of the SFJ and tributaries as a routine step to be performed along with RFA to avert thrombus propagation into the CFV and to deal with the risk of recanalization. With increased experience, this maneuver has proved unnecessary because it did not alter outcome for thromboembolic events.[32] With the aim to determine the clinical value of adjunctive proximal vein ligation, Gradman[30] created a survey for physicians performing endovenous GSV ablation procedures. Of 21,965 GSV obliteration procedures done by 22 practitioners, two cases of PE (0.009%) and 34 of DVT (0.15%) were reported. Of the 34 patients with DVT, at least 11 had duplex evidence of thrombus extension into the CFV that was asymptomatic and five had a calf muscle veins DVT. No difference was noted between ligated and nonligated GSVs in DVT occurrence.

Although a history of DVT is generally considered a contraindication for endovenous ablation procedures, we were unable to identify a study that directly addressed the question whether RFA is safe in this group of patients. In a review of literature, we found that main etiology of CVI (E of CEAP classification) was secondary to a previous DVT (Es) only in about 2% in RFA series[5]; more often, the cause of chronic venous insufficiency was not reported. In the Endovenous Radiofrequency Obliteration Versus Ligation and Stripping (EVOLVeS) study,[2] as well as other studies,[8,9,10] an episode of previous DVT was one of the main exclusion criteria for endovenous GSV ablation. Therefore, the question remained open and prompted us to perform this study.

To date, there is no reliable test and there are no definitive criteria able to quantify deep venous obstruction. Ascending phlebography can provide valuable information on the patency of the deep system; however, the test is invasive, is associated with a number of risks—including DVT—and is mainly indicated in cases of planned deep venous reconstructions. Duplex scan is rather performed if only superficial venous surgery is being considered.

The traditional admonition against removal of the GSV in post-thrombotic limbs has been re-examined by Raju et al.[33] Saphenectomy was clinically well tolerated in limbs with or without deep venous obstruction, and no difference in outcome was noted as measured by objective tests for obstruction. Improvement in reflux and calf venous pump function was largely similar. Saphenous ablation may benefit patients with post-thrombotic syndrome with mixed deep obstruction or superficial reflux and should not be denied to this group of patients.

In a study by Neglén et al,[34] 99 limbs with concomitant superficial reflux and deep venous obstruction (41% with previous DVT) were treated by combined saphenous ablation (27 by RFA) and iliac stent placement. Early DVT occurred in only one patient in the contralateral iliofemoral vein 27 days after the intervention. It is unclear whether this was primary or post-thrombotic venous disease.

To our knowledge, only one report, by our group,[4] has analyzed risk factors for AT events after RFA techniques, probably due to the low incidence of this complication in most of the other series. After 73 RFA procedures, no difference was found between the occurrence of DVT in patients who underwent a combined procedure (RFA and varicose vein excision) compared with patients who underwent GSV RFA alone ($P = .7$).

Two separate reports on combined GSV EVLA and phlebectomy in the treatment of varicose veins found a low DVT rate of 0% and 0.13%, respectively.[35,36] In a recent

report from the Michigan Venous Study Group on 443 limbs,[24] however, EVLA alone in 308 limbs (69.5%) and combined with phlebectomy or perforator ligation in 135 limbs (30.5%) had an overall 7.9% incidence of AT events (0.7% true DVTs and 7.2% SFJ thrombus extensions). The true DVT rate was 2.2% for combined EVLA/venous operations and 0% for isolated EVLA ($P = .028$); the rate of SFJ thrombus extension was 5.9% for combined EVLA/venous operations vs 7.8% for isolated EVLA ($P = .554$). The rate of AT events after EVLA and their higher incidence after concomitant venous procedures are in agreement with our findings.

One can speculate that the increased incidence of AT events after RFA and concomitant venous operations may be attributed to prolonged immobilization during and after the procedure due to increased operative time, type of anesthesia, and postoperative pain. It is also possible that because most of the concomitant operations in our series were performed during the first study period, several other confounding factors might have affected the results. In line with this observation is the result of the multivariate analysis, where this risk factor did not retain statistical significance as an independent variable.

Treatment of incompetent perforators is still a matter of controversy. The role of incompetent perforators ablation alone or with GSV treatment awaits results of properly conducted randomized controlled trials.[37] Our patient population consisted of a large number of elderly individuals (mean age, 60 ± 15 years) with significant comorbidities. At the time of the study, perforator reflux was investigated and treated only in a limited number of patients with long-standing nonhealing leg ulcers. Conservative treatment was not successful in these patients, and they were willing and fit to undergo surgical perforator interruption. More recently, with the introduction of the RFA Stylet (VNUS Medical Technologies Inc, San Jose, Calif), which does not require anesthesia or sedation, we have been able to treat an increasing number of patients with perforator vein reflux.

After GSV ablation, lower extremity varicose veins often disappear or visibly regress,[10,38] and their elimination by sclerotherapy or stab avulsion is required in <35% of patients. In our early experience, elimination of GSV reflux and phlebectomies of symptomatic or unsightly varicose veins were performed mostly at the same time. Currently, most of our patients receive RFA alone as the initial operative approach to superficial vein reflux. Any significant varicosities that persist >3 to 6 months are treated by sclerotherapy or phlebectomies (<30%, unpublished data).

This is a retrospective study with certain limitations. Our protocol included a first follow-up visit 1 week after the procedure. Patients were asked to return for further duplex studies, but compliance was 65%. A mean midterm follow-up of 53 days is reasonable to detect acute/subacute events but not delayed complications or late results. As such, the presented data focused on early results rather than longer-term follow-up.

It is possible that postphlebitic GSVs are at higher risk of developing DVT after the RFA procedure due to increased thrombogenicity of the endothelium. By history, patients in this study who reported an episode of phlebitis had been treated only with a short course of mild analgesics during the acute episode. Unfortunately, not enough information on exact location of previous SVT was available because this was a retrospective study and we were unable to determine if it had involved the GSV. Several risk factors are associated with SVT, and a strong correlation is seen with certain thrombophilias.[39] Testing for hypercoagulable states before endovenous ablation may therefore be indicated in patients with a history of spontaneous onset of SVT.

One of the main limitations of this study (and of most reports on post-thrombotic limbs) is that the definition of post-thrombotic venous stenosis remains obscure, and no reliable tests are available to confirm the presence of such lesions. Most thrombosed venous segments recanalize during the next 6 to 12 months after an episode of DVT, leading to chronic luminal changes that may cause partial obstruction. Unfortunately, the diagnostic evaluation of secondary chronic venous disease by duplex ultrasound imaging is not as well defined as for primary venous disease; thus, there are no reliable criteria to confirm the presence of such lesions.[40] This remains an elusive area in duplex scanning, represents a challenging subject for future studies, and might have affected our results due to an unavoidable bias in selecting the limbs that had a previous DVT.

DVT prophylaxis was administered in only in a few patients with a history of DVT, at the surgeon's discretion; these data were not included in the analysis. A recent study found the use of low-molecular-weight heparin for perioperative prophylaxis by a risk-adjusted protocol in patients undergoing EVLA did not have a significant effect on thrombotic complications.[24] Until further prospective, randomized studies on DVT prophylaxis in this subset of patients become available, we do not think the use of periprocedural anticoagulation is justified because it may be associated with bleeding complications. Patients with a history of DVT are not commonly tested for factor V mutation or other types of hypercoagulability before superficial venous surgery, and it is not routine in our practice. In the future, however, such information may be useful in stratifying patients at risk for postprocedural DVT, especially those with previous thromboembolic events, and could be the subject for further studies.

CONCLUSIONS

This experience shows that RFA of the GSV can be safely performed in patients with a history of venous thromboembolic events, and it should be offered as an alternative to surgical procedures for symptomatic superficial vein reflux. These data call attention to an increased incidence of AT events when large- diameter GSVs are treated.

AUTHOR CONTRIBUTIONS

Conception and design: AP, AH, AS, EA
Analysis and interpretation: AP, NM, SA, EA
Data collection: AP, NM, AH, SA
Writing the article: AP, EA

Critical revision of the article: AP, NM, AH, AS, SA, EA
Final approval of the article: AP, NM, AH, AS, SA, EA
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